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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,918	04/09/2007	Rajendra Narayanrao Kankan	PAC/22609 US (4137-01300)	6584
30652	7590	03/16/2009	EXAMINER	
CONLEY ROSE, P.C. 5601 GRANITE PARKWAY, SUITE 750 PLANO, TX 75024			BLANCHI, KRISTIN A	
			ART UNIT	PAPER NUMBER
			1626	
			MAIL DATE	DELIVERY MODE
			03/16/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/599,918	<b>Applicant(s)</b> KANKAN ET AL.	
	<b>Examiner</b> KRISTIN BIANCHI	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,36-46 and 48-67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,36-46 and 48-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/15/2007</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1, 36-46 and 48-67 are currently pending in the instant application.

Claims 1, 36-46 and 48-67 are rejected.

#### ***Information Disclosure Statement***

The information disclosure statement filed on December 15, 2007 has been considered and a signed copy of form 1449 is enclosed herewith.

#### ***Election/Restrictions and Amendment***

Applicants' election of Group I in the response filed on December 18, 2008 is acknowledged. The amendment filed on December 18, 2008 has been fully considered and entered into the application. Since Applicants have amended the claims of Groups II-IV to depend from the elected Group I, Groups II-IV have been rejoined with Group I (i.e. claims 1, 36-46 and 48-67 have been searched and examined in their entirety).

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43, 48 and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 recites the limitation "wherein the aralkyl group is a **benzyl group** or a substituted benzyl group" in lines 6 and 7 on page 4. There is insufficient antecedent basis for this limitation in the claim. The claim from which claim 43 depends or claim 1

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does not recite an unsubstituted benzyl or a benzyl group as an option for the aralkyl group. Appropriate correction is required.

Claims 48 and 64 appear to be duplicates of claims 43 and 57, respectively, or they do not appear to further limit claim 1. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 36-46 and 48-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,914,214.

#### ***Determining the scope and contents of the prior art***

US Patent No. 4,914,214 (Vincent et al.) discloses the conversion of S-indole-2-carboxylic acid to (2S,3aS,7aS)-octahydroindole-2-carboxylic acid by hydrogenation in methanol through the use of a rhodium (5%) catalyst (column 7, Stage 1E). Vincent et al. also discloses the condensation of ethyl N-norvalinate hydrochloride and pyruvic acid to yield N-[(S)-1-carbethoxybutyl]-(S)-alanine wherein the condensation is carried out under catalytic hydrogenation in the presence of palladium on carbon as the catalyst. Any inorganic salts present in the reaction medium are removed by filtration to obtain a filtrate, the filtrate is

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concentrated and N-[(S)-1-carbethoxybutyl]-(S)-alanine is isolated by precipitation by the addition of acetonitrile (column 8, Stage 2B). Vincent also discloses the reaction of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid, p-toluene sulphonic acid, benzyl alcohol and toluene to form the aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (column 8, Stage 3A). Triethylamine is added to the product of Stage 3A and the benzyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is coupled with N-[(S)-1-carbethoxybutyl]-(S)-alanine in the presence of DCC and HBT0 (column 8, Stage 3B). The product of Stage 3B is deprotected by hydrogenolysis of the benzyl ester of the (2S,3aS,7aS)-1-{2-[1-(ethoxycarbonyl)-(S)-butylamino]-(S)-propinoyl]-octahydroindole-2-carboxylic acid in the presence of palladium on carbon (column 8 and column 9, Stage 3C). Finally, the perindopril is converted to the tert butyl amine salt in Stage 3D (column 9).

***Ascertaining the differences between the prior art and the claims at issue***

There are a few differences between the synthesis of the tert butyl amine salt of perindopril disclosed in Vincent et al. and the process of the instant claims (i.e. a substituted benzyl is used as the protecting group in the instant claims whereas an unsubstituted benzyl is used as the protecting group in Vincent et al. and the amount of pressure used in the hydrogenation procedures is higher in Vincent et al. than in the instant claims, etc.).

***Establishing a prima facie case of obviousness***

It would have been obvious to one of ordinary skill in the art at the time of the invention to experiment with the reaction conditions disclosed in Vincent et al. (i.e. to test out the hydrogenation reactions at different pressures and to experiment with different protecting groups) in an attempt to find the optimal reaction conditions for preparing perindopril or the tert-butylamine salt of perindopril and to arrive at the process of the instant claims. Especially since it was known in the art that the tert-butylamine salt of perindopril has interesting pharmacological properties (i.e. it inhibits certain enzymes, see column I of Vincent et al.). The motivation would have been to find the optimal reaction conditions for producing perindopril or the tert-butylamine salt of perindopril. One of ordinary skill would have a reasonable expectation of success in practicing the instantly claimed process.

Also, the courts have stated that a change in process conditions of an old process does not impart patentability in the absence of unexpected results. In re Boesch, 205 USPQ 215 (1980). In re Aller et al. (CCPA 1955) 220 F2d 454.

Thus, a *prima facie* case of obviousness has been established.

***Conclusion***

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/  
Primary Examiner, Art Unit 1626

Kristin Bianchi  
Examiner  
Art Unit 1626

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